09/526,193 Search Strategy/Results

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FILE 'MEDLINE' ENTERED AT 09:01:08 ON 14 MAY 2002

FILE 'AGRICOLA' ENTERED AT 09:01:08 ON 14 MAY 2002

FILE 'CAPLUS' ENTERED AT 09:01:08 ON 14 MAY 2002
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FILE 'BIOSIS' ENTERED AT 09:01:08 ON 14 MAY 2002
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=> s abc1
L1          444 ABC1

=> s l1 and (mammalian or human or mouse or murine or sapien#)
L2          296 L1 AND (MAMMALIAN OR HUMAN OR MOUSE OR MURINE OR SAPIEN#)

=> s l2 and (inhibit? or modulat? or activat? or bind? or interact?)
   5 FILES SEARCHED...
L3          246 L2 AND (INHIBIT? OR MODULAT? OR ACTIVAT? OR BIND? OR INTERACT?)


=> s l3 not py>1999
L4           82 L3 NOT PY>1999

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5           34 DUP REM L4 (48 DUPLICATES REMOVED)

=>
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L5 ANSWER 1 OF 34 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000006295 MEDLINE
DOCUMENT NUMBER: 20006295 PubMed ID: 10535983
TITLE: **Human** ATP-**binding** cassette transporter 1 (**ABC1**): genomic organization and identification of the genetic defect in the original Tangier disease kindred.
AUTHOR: Remaley A T; Rust S; Rosier M; Knapper C; Naudin L; Broccardo C; Peterson K M; Koch C; Arnould I; Prades C; Duverger N; Funke H; Assman G; Dinger M; Dean M; Chimini G; Santamarina-Fojo S; Fredrickson D S; Denefle P; Brewer H B Jr
CORPORATE SOURCE: National Institutes of Health, National Heart, Lung and Blood Institute, Bethesda, MD 20892, USA.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Oct 26) 96 (22) 12685-90. Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991210
AB Tangier disease is characterized by low serum high density lipoproteins and a biochemical defect in the cellular efflux of lipids to high density lipoproteins. **ABC1**, a member of the ATP-**binding** cassette family, recently has been identified as the defective gene in Tangier disease. We report here the organization of the **human** **ABC1** gene and the identification of a mutation in the **ABC1** gene from the original Tangier disease kindred. The organization of the **human** **ABC1** gene is similar to that of the **mouse** **ABC1** gene and other related ABC genes. The **ABC1** gene contains 49 exons that range in size from 33 to 249 bp and is over 70 kb in length. Sequence analysis of the **ABC1** gene revealed that the proband for Tangier disease was homozygous for a deletion of nucleotides 3283 and 3284 (TC) in exon 22. The deletion results in a frameshift mutation and a premature stop codon starting at nucleotide 3375. The product is predicted to encode a nonfunctional protein of 1,084 aa, which is approximately half the size of the full-length **ABC1** protein. The loss of a MnlI restriction site, which results from the deletion, was used to establish the genotype of the rest of the kindred. In summary, we report on the genomic organization of the **human** **ABC1** gene and identify a frameshift mutation in the **ABC1** gene of the index case of Tangier disease. These results will be useful in the future characterization of the structure and function of the **ABC1** gene and the analysis of additional **ABC1** mutations in patients with Tangier disease.

L5 ANSWER 2 OF 34 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:684452 CAPLUS
DOCUMENT NUMBER: 131:349697
TITLE: Effluxed lipids: Tangier Island's latest export
AUTHOR(S): Freeman, Mason W.
CORPORATE SOURCE: Lipid Metabolism Unit, Massachusetts General Hospital and Harvard Medical School, Boston, MA, 02114, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1999), 96(20), 10950-10952
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 32 refs. Current findings of Y. Takahashi and J.D. Smith (1999) propose a novel mechanism through which apolipoprotein A-I (apoAI) appears to remove cholesterol from cells, a process that is defective in individuals with Tangier disease. Recently, an ATP **binding** cassette transporter (**ABC1**) was shown to be mutated in patients with Tangier disease. These discoveries and their implications and inter-relationships are discussed.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:2936 BIOSIS
DOCUMENT NUMBER: PREV200000002936
TITLE: Role of **ABC1** gene in cholesterol efflux and atheroprotection.
AUTHOR(S): Owen, James S. (1)
CORPORATE SOURCE: (1) Department of Medicine, Royal Free and University College Medical School, University College London, London, NW3 2PF UK
SOURCE: Lancet (North American Edition), (Oct. 23, 1999) Vol. 354, No. 9188, pp. 1402-1403.
ISSN: 0099-5355.
DOCUMENT TYPE: Article
LANGUAGE: English

L5 ANSWER 4 OF 34 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2000001430 MEDLINE
DOCUMENT NUMBER: 20001430 PubMed ID: 10533863
TITLE: Mutations in the **ABC1** gene in familial HDL deficiency with defective cholesterol efflux.
COMMENT: Comment in: Lancet. 1999 Oct 23;354(9188):1402-3
AUTHOR: Marcil M; Brooks-Wilson A; Clee S M; Roomp K; Zhang L H; Yu L; Collins J A; van Dam M; Molhuizen H O; Loubster O; Ouellette B F; Sensen C W; Pichter K; Mott S; Denis M; Boucher B; Pimstone S; Genest J Jr; Kastelein J J; Hayden M R
CORPORATE SOURCE: Xenon Bioresearch Inc, NRC Innovation Centre, Vancouver, British Columbia, Canada.
SOURCE: LANCET, (1999 Oct 16) 354 (9187) 1341-6.
Journal code: L0S; 2985213R. ISSN: 0140-6736.

PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000209
Entered Medline: 19991119

AB BACKGROUND: A low concentration of HDL cholesterol is the most common lipoprotein abnormality in patients with premature atherosclerosis. We have shown that Tangier disease, a rare and severe form of HDL deficiency characterised by a biochemical defect in cellular cholesterol efflux, is caused by mutations in the ATP-**binding**-cassette (**ABC1**) gene. This gene codes for the cholesterol-efflux regulatory protein (CERP). We investigated the presence of mutations in this gene in patients with familial HDL deficiency. METHODS: Three French-Canadian families and one Dutch family with familial HDL deficiency were studied. Fibroblasts from the proband of each family were defective in cellular cholesterol efflux. Genomic DNA of each proband was used for mutation detection with primers flanking each exon of the **ABC1** gene, and for sequencing of the entire coding region of the gene. PCR and restriction-fragment length polymorphism assays specific to each mutation were used to investigate segregation of the mutation in each family, and to test for absence of the mutation in DNA from normal controls. FINDINGS: A different mutation was detected in **ABC1** in each family studied. Each mutation either created a stop codon predicted to result in truncation of CERP, or altered a conserved aminoacid residue. Each mutation segregated with low concentrations of HDL-cholesterol in the family, and was not observed in more than 500 control chromosomes tested. INTERPRETATION: These data show that mutations in **ABC1** are the major cause of familial HDL deficiency associated with defective cholesterol efflux, and that CERP has an essential role in the formation of HDL. Our findings highlight the potential of **modulation** of **ABC1** as a new route for increasing HDL concentrations.

L5 ANSWER 5 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:145545 BIOSIS
DOCUMENT NUMBER: PREV199900145545
TITLE: Sequence divergence of the RNA polymerase shared subunit ABC14.5 (Rpb8) selectively affects RNA polymerase III assembly in Saccharomyces cerevisiae.
AUTHOR(S): Voutsina, Alexandra; Riva, Michel; Carles, Christophe; Alexandraki, Despina (1)
CORPORATE SOURCE: (1) Inst. Molecular Biol. Biotechnology, P.O. Box 1527, Heraklion 711 10 Crete Greece
SOURCE: Nucleic Acids Research, (Feb. 15, 1999) Vol. 27, No. 4, pp. 1047-1055.
ISSN: 0305-1048.
DOCUMENT TYPE: Article
LANGUAGE: English

AB ABC14.5 (Rpb8) is a eukaryotic subunit common to all three nuclear RNA polymerases. In Saccharomyces cerevisiae, ABC14.5 (Rpb8) is essential for cell viability, however its function remains unknown. We have cloned and characterized the Schizosaccharomyces pombe rpb8+ cDNA. We found that S. pombe rpb8, unlike the similarly diverged **human** orthologue, cannot substitute for S. cerevisiae ABC14.5 in vivo. To obtain information on the function of this RNA polymerase shared subunit we have used S. pombe rpb8 as a naturally altered molecule in heterologous expression assays in S. cerevisiae. Amino acid residue differences within the 67 N-terminal residues contribute to the functional distinction of the two yeast orthologues in S. cerevisiae. Overexpression of the S. cerevisiae largest subunit of RNA polymerase III C160 (Rpc1) allows S. pombe rpb8 to functionally replace **ABC1** 4.5 in S. cerevisiae, suggesting a specific genetic **interaction** between the S. cerevisiae ABC14.5 (Rpb8) and C160 subunits. We provide further molecular and biochemical evidence showing that the heterologously expressed S. pombe rpb8 molecule selectively affects RNA polymerase III but not RNA polymerase I complex assembly. We also report the identification of a S. cerevisiae ABC14.5-G120D mutant which affects RNA polymerase III.

L5 ANSWER 6 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:3408 BIOSIS
DOCUMENT NUMBER: PREV200000003408
TITLE: Stereo-specific **activation** of the complement system by phosphatidylserine (PS) appearing on apoptotic cells.
AUTHOR(S): Mevorach, Dror (1); Prolekis, Ina (1); Shapira, Itzhak (1)
CORPORATE SOURCE: (1) Tel-Aviv Israel
SOURCE: Arthritis & Rheumatism, (Sept., 1999) Vol. 42, No. 9 SUPPL., pp. S406.
Meeting Info.: 63rd Annual Scientific Meeting of the American College of Rheumatology and the 34th Annual Scientific Meeting of the Association of Rheumatology Health Professionals Boston, Massachusetts, USA November 13-17, 1999
ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L5 ANSWER 7 OF 34 MEDLINE
ACCESSION NUMBER: 2000050105 MEDLINE
DOCUMENT NUMBER: 20050105 PubMed ID: 10581369
TITLE: The ABCA subclass of **mammalian** transporters.
AUTHOR: Broccardo C; Luciani M; Chimini G
CORPORATE SOURCE: Centre d'Immunologie de Marseille-Luminy, Parc Scientifique de Luminy, 13288, Marseille, France.
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (1999 Dec 6) 1461 (2) 395-404. Ref: 45
Journal code: A0W; 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000114
Last Updated on STN: 20000114
Entered Medline: 20000106

AB We describe here a subclass of **mammalian** ABC transporters, the ABCA subfamily. This is a unique group that, in contrast to any other **human** ABC transporters, lacks a structural counterpart in yeast. The structural hallmark of the ABCA subfamily is the presence of a stretch of hydrophobic amino acids thought to span the membrane within the putative regulatory (R) domain. As for today, four ABCA transporters have been fully characterised but 11 ABCA-encoding genes have been identified. ABCA-specific motifs in the nucleotide **binding** folds can be detected when analysing the conserved sequences among the different members. These motifs may reveal functional constraints exclusive to this group of ABC transporters.

L5 ANSWER 8 OF 34 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1999096930 MEDLINE
DOCUMENT NUMBER: 99096930 PubMed ID: 9878413
TITLE: Identification and characterization of a **mammalian** mitochondrial ATP-**binding** cassette membrane protein.
AUTHOR: Hogue D L; Liu L; Ling V
CORPORATE SOURCE: BC Cancer Research Centre, Vancouver, British Columbia, V5Z 4L3, Canada.
SOURCE: JOURNAL OF MOLECULAR BIOLOGY, (1999 Jan 8) 285 (1) 379-89.
Journal code: J6V; 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF047690
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990324
Last Updated on STN: 19990324
Entered Medline: 19990311

AB Membrane proteins of the ATP-**binding** cassette (ABC) superfamily are involved in the transport of diverse substrates across organellar and plasma membranes of the **mammalian** cell. Most **human** ABC proteins identified to date are associated with genetically linked diseases or clinically relevant phenotypes. We describe a new **human** half-molecule ABC protein, designated M-**ABC1**, that contains a predicted single membrane and ATP-**binding** cassette domain. M-**ABC1** is localized to membranes of the mitochondria and its transcript is expressed in all tissues. The N-terminal region of the M-**ABC1** protein was shown to function independently as a mitochondrial signal sequence by its ability to target the green fluorescent protein to the mitochondria. The monomeric 60 kDa M-**ABC1** protein was chemically crosslinked in vivo into a major protein species of 120-130 kDa, thereby confirming that M-**ABC1** exists within a higher ordered ABC protein complex. A dominant negative repression approach using M-**ABC1** protein with site-directed mutations in its Walker A motif revealed that the mutant protein was rapidly degraded and indicated that the intact Walker A motif of M-**ABC1** was required for its stability. The identification of M-**ABC1** extends the known distribution of members of the ABC protein family into the **mammalian** mitochondrion.

L5 ANSWER 9 OF 34 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 1999364413 MEDLINE
DOCUMENT NUMBER: 99364413 PubMed ID: 10431238
TITLE: Tangier disease is caused by mutations in the gene encoding ATP-**binding** cassette transporter 1.
COMMENT: Comment in: Nat Genet. 1999 Aug;22(4):316-8
AUTHOR: Rust S; Rosier M; Funke H; Real J; Amoura Z; Piette J C; Deleuze J F; Brewer H B; Duverger N; Denefle P; Assmann G
CORPORATE SOURCE: Institut fur Arteriosklerosеforschung an der Westfalischen Wilhelms-Universitat Munster, Germany..
Rusts@uni-muenster.de
SOURCE: NATURE GENETICS, (1999 Aug) 22 (4) 352-5.
Journal code: BRO; 9216904. ISSN: 1061-4036.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF165281; GENBANK-AF165282; GENBANK-AF165283; GENBANK-AF165284; GENBANK-AF165285; GENBANK-AF165286; GENBANK-AF165287; GENBANK-AF165288; GENBANK-AF165289; GENBANK-AF165290; GENBANK-AF165291; GENBANK-AF165292; GENBANK-AF165293; GENBANK-AF165294; GENBANK-AF165295; GENBANK-AF165296; GENBANK-AF165297; GENBANK-AF165298; GENBANK-AF165299; GENBANK-AF165300; GENBANK-AF165301; GENBANK-AF165302; GENBANK-AF165303; GENBANK-AF165304; GENBANK-AF165305; GENBANK-AF165306; GENBANK-AF165307; GENBANK-AF165308; GENBANK-AF165309; GENBANK-AF165310
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990910
Last Updated on STN: 19990910
Entered Medline: 19990826

AB Tangier disease (TD) was first discovered nearly 40 years ago in two siblings living on Tangier Island. This autosomal co-dominant condition is characterized in the homozygous state by the absence of HDL-cholesterol (HDL-C) from plasma, hepatosplenomegaly, peripheral neuropathy and frequently premature coronary artery disease (CAD). In heterozygotes, HDL-C levels are about one-half those of normal individuals. Impaired cholesterol efflux from macrophages leads to the presence of foam cells throughout the body, which may explain the increased risk of coronary heart disease in some TD families. We report here refining of our previous linkage of the TD gene to a 1-cM region between markers D9S271 and D9S1866 on chromosome 9q31, in which we found the gene encoding **human** ATP cassette-**binding** transporter 1 (**ABC1**). We also found a change in **ABC1** expression level on cholesterol loading

of phorbol ester-treated THP1 macrophages, substantiating the role of **ABC1** in cholesterol efflux. We cloned the full-length cDNA and sequenced the gene in two unrelated families with four TD homozygotes. In the first pedigree, a 1-bp deletion in exon 13, resulting in truncation of the predicted protein to approximately one-fourth of its normal size, co-segregated with the disease phenotype. An in-frame insertion-deletion in exon 12 was found in the second family. Our findings indicate that defects in **ABC1**, encoding a member of the ABC transporter superfamily, are the cause of TD.

L5 ANSWER 10 OF 34 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1999364412 MEDLINE
DOCUMENT NUMBER: 99364412 PubMed ID: 10431237
TITLE: The gene encoding ATP-**binding** cassette transporter 1 is mutated in Tangier disease.
COMMENT: Comment in: Nat Genet. 1999 Aug;22(4):316-8
AUTHOR: Bodzioch M; Orso E; Klucken J; Langmann T; Bottcher A; Diederich W; Drobnik W; Barlage S; Buchler C; Porsch-Ozcurumez M; Kaminski W E; Hahmann H W; Oette K; Rothe G; Aslanidis C; Lackner K J; Schmitz G
CORPORATE SOURCE: Institute for Clinical Chemistry and Laboratory Medicine, University of Regensburg, Germany.
SOURCE: NATURE GENETICS, (1999 Aug) 22 (4) 347-51. Journal code: BRO; 9216904. ISSN: 1061-4036.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ012376
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990910
Last Updated on STN: 19990910
Entered Medline: 19990826

AB Tangier disease (TD) is an autosomal recessive disorder of lipid metabolism. It is characterized by absence of plasma high-density lipoprotein (HDL) and deposition of cholesteryl esters in the reticulo-endothelial system with splenomegaly and enlargement of tonsils and lymph nodes. Although low HDL cholesterol is associated with an increased risk for coronary artery disease, this condition is not consistently found in TD pedigrees. Metabolic studies in TD patients have revealed a rapid catabolism of HDL and its precursors. In contrast to normal mononuclear phagocytes (MNP), MNP from TD individuals degrade internalized HDL in unusual lysosomes, indicating a defect in cellular lipid metabolism. HDL-mediated cholesterol efflux and intracellular lipid trafficking and turnover are abnormal in TD fibroblasts, which have a reduced in vitro growth rate. The TD locus has been mapped to chromosome 9q31. Here we present evidence that TD is caused by mutations in **ABC1**, encoding a member of the ATP-**binding** cassette (ABC) transporter family, located on chromosome 9q22-31. We have analysed five kindreds with TD and identified seven different mutations, including three that are expected to impair the function of the gene product. The identification of **ABC1** as the TD locus has implications for the understanding of cellular HDL metabolism and reverse cholesterol transport, and its association with premature cardiovascular disease.

L5 ANSWER 11 OF 34 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 1999364411 MEDLINE
DOCUMENT NUMBER: 99364411 PubMed ID: 10431236
TITLE: Mutations in **ABC1** in Tangier disease and familial high-density lipoprotein deficiency.
COMMENT: Comment in: Nat Genet. 1999 Aug;22(4):316-8
AUTHOR: Brooks-Wilson A; Marcil M; Clee S M; Zhang L H; Roomp K; van Dam M; Yu L; Brewer C; Collins J A; Molhuizen H O; Loubser O; Ouelette B F; Fichter K; Ashbourne-Excoffon K J; Sensen C W; Scherer S; Mott S; Denis M; Martindale D; Frohlich J; Morgan K; Koop B; Pimstone S; Kastelein J J; Hayden M R; +
CORPORATE SOURCE: Xenon Bioresearch Inc., NRC Innovation Centre, Vancouver, British Columbia, Canada.
SOURCE: NATURE GENETICS, (1999 Aug) 22 (4) 336-45. Journal code: BRO; 9216904. ISSN: 1061-4036.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ012376; GENBANK-X75926
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990910
Last Updated on STN: 19990910
Entered Medline: 19990826

AB Genes have a major role in the control of high-density lipoprotein (HDL) cholesterol (HDL-C) levels. Here we have identified two Tangier disease (TD) families, confirmed 9q31 linkage and refined the disease locus to a limited genomic region containing the gene encoding the ATP-**binding** cassette transporter (**ABC1**). Familial HDL deficiency (FHA) is a more frequent cause of low HDL levels. On the basis of independent linkage and meiotic recombinants, we localized the FHA locus to the same genomic region as the TD locus. Mutations in **ABC1** were detected in both TD and FHA, indicating that TD and FHA are allelic. This indicates that the protein encoded by **ABC1** is a key gatekeeper influencing intracellular cholesterol transport, hence we have named it cholesterol efflux regulatory protein (CERP).

L5 ANSWER 12 OF 34 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 2000050095 MEDLINE
DOCUMENT NUMBER: 20050095 PubMed ID: 10581359
TITLE: An inventory of the **human** ABC proteins.
AUTHOR: Klein I; Sarkadi B; Varadi A
CORPORATE SOURCE: Institute of Enzymology, Biological Research Center, Hungarian Academy of Sciences, H-1502, Budapest, Hungary.
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (1999 Dec 6) 1461 (2) 237-62. Ref: 138
Journal code: A0W; 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands

Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000114
Last Updated on STN: 20000114
Entered Medline: 20000106

AB Currently 30 **human** ABC proteins are represented by full sequences in various databases, and this paper provides a brief overview of these proteins. ABC proteins are composed of transmembrane domains (TMDs), and nucleotide **binding** domains (NBDs, or ATP-**binding** cassettes, ABSs). The arrangement of these domains, together with available membrane topology models of the family members, are presented. Based on their sequence similarity scores, the members of the **human** ABC protein family can be grouped into eight subfamilies. At present the MDR/TAP, the ALD, the MRP/CFTR, the **ABC1**, the White, the RNAseL **inhibitor**, the ANSA, and the GCN20 subfamilies are identified. Mutations of many **human** ABC proteins are known to be causative in inherited diseases, and a short description of the molecular pathology of these ABC gene-related genetic diseases is also provided.

L5 ANSWER 13 OF 34 MEDLINE
ACCESSION NUMBER: 2000191593 MEDLINE
DOCUMENT NUMBER: 20191593 PubMed ID: 10725792
TITLE: ATP-**binding** cassette transporter A1 (ABCA1) in macrophages: a dual function in inflammation and lipid metabolism?.
AUTHOR: Schmitz G; Kaminski W E; Porsch-Ozcurumez M; Klucken J; Orso E; Bodzioch M; Buchler C; Drobnik W
CORPORATE SOURCE: Institute of Clinical Chemistry and Laboratory Medicine, University of Regensburg, Germany.. gerd.schmitz@klinik.uni-regensburg.de
SOURCE: PATHOBIOLOGY, (1999) 67 (5-6) 236-40.
Journal code: AF6; 9007504. ISSN: 1015-2008.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000518
Last Updated on STN: 20000518
Entered Medline: 20000510

AB **Activated** lipid-laden macrophages in the vascular wall are key **modulators** of the inflammatory processes underlying atherosclerosis. We demonstrate here that the ATP-**binding** cassette (ABC) transporter ABCA1 is induced during differentiation of **human** monocytes into macrophages. ABCA1 has been implicated in macrophage interleukin-1beta secretion and apoptosis. Moreover, ABCA1 mRNA and protein levels are strongly upregulated by uptake of modified LDL and downregulated by HDL(3)-mediated lipid efflux in macrophages. Mutation analysis in patients with the classical Tangier disease (TD), a monogenetic disorder characterized by hypersplenism, macrophage accumulation and deposition of cholesteryl esters in the reticuloendothelial system, low plasma HDL and premature atherosclerosis, revealed deleterious mutations in their ABCA1 gene. The localization pattern of the mutations within the ABCA1 protein appears to determine the tropism for either the reticuloendothelial system, as seen in the classical TD phenotype, or the artery wall, as in the case of HDL deficiency in the absence of splenomegaly. In a comprehensive analysis of the expression and regulation of all currently known **human** ABC transporters, we identified additional cholesterol-responsive genes that are induced during monocyte differentiation into macrophages. Our results indicate a dual regulatory function for ABCA1 in macrophage lipid metabolism and inflammation.

L5 ANSWER 14 OF 34 BIOSIS
ACCESSION NUMBER: 1999:506445 BIOSIS
DOCUMENT NUMBER: PREV199900506445
TITLE: Mutations in transportin (**ABC1**) in Tangier disease and familial HDL deficiency.
AUTHOR(S): Brooks-Wilson, A. R. (1); Marcil, M. (1); Clee, S. M.; Zhang, L.-H. (1); Roomp, K. (1); van Dam, M. J.; Yu, L.; Brewer, C.; Collins, J. A. (1); Molhuizen, H.O.F.; Ouellette, B.F.F.; Sensen, C. W. (1); Martindale, D.; Prohlich, J.; Morgan, K.; Koop, B.; Pimstone, S. (1); Kastelein, J.J.P.; Genest, J., Jr.; Hayden, M. R.
CORPORATE SOURCE: (1) Xenon Bioresearch, Vancouver Canada
SOURCE: American Journal of Human Genetics, (Oct., 1999) Vol. 65, No. 4, pp. A34.
Meeting Info.: 49th Annual Meeting of the American Society of Human Genetics San Francisco, California, USA October 19-23, 1999 The American Society of Human Genetics . ISSN: 0002-9297.
DOCUMENT TYPE: Conference
LANGUAGE: English

L5 ANSWER 15 OF 34 BIOSIS
ACCESSION NUMBER: 1999:506444 BIOSIS
DOCUMENT NUMBER: PREV199900506444
TITLE: A defective gene associated with atherosclerosis: Tangier disease is caused by mutations in the ATP **binding** cassette transporter 1 (**ABC1**.
AUTHOR(S): Rust, S. (1); Rosier, M.; Funke, H. (1); Real, J.; Amoura, Z.; Piette, J.-C.; Deleuze, J.-F.; Brewer, H. B.; Duverger, N.; Denefle, P.; Assmann, G. (1)
CORPORATE SOURCE: (1) Molecular Genetics, Inst. f. Arteriosclerosis Res., NRW, Muenster Germany
SOURCE: American Journal of Human Genetics, (Oct., 1999) Vol. 65, No. 4, pp. A33.
Meeting Info.: 49th Annual Meeting of the American Society

of Human Genetics San Francisco, California, USA October 19-23, 1999 The American Society of Human Genetics . ISSN: 0002-9297.
DOCUMENT TYPE: Conference
LANGUAGE: English

L5 ANSWER 16 OF 34 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 1999194549 MEDLINE
DOCUMENT NUMBER: 99194549 PubMed ID: 10092505
TITLE: Molecular cloning of the **human** ATP-**binding** cassette transporter 1 (hABC1): evidence for sterol-dependent regulation in macrophages.
AUTHOR: Langmann T; Klucken J; Reil M; Liebisch G; Luciani M F; Chimini G; Kaminski W E; Schmitz G
CORPORATE SOURCE: Institute for Clinical Chemistry and Laboratory Medicine, University of Regensburg, Regensburg, 93042, Germany.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1999 Apr 2) 257 (1) 29-33.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ012376
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990525
Last Updated on STN: 19990525
Entered Medline: 19990511
AB We have cloned the full-length cDNA for the **human** ATP **binding** cassette transporter 1 (hABC1). The 6603-bp open reading frame encodes a polypeptide of 2201 amino acids resulting in a deduced molecular weight of 220 kDa. The hABC1 cDNA is highly homologous (62%) to the **human** rim ABC transporter (ABCR). hABC1 is expressed in a variety of **human** tissues with highest expression levels found in placenta, liver, lung, adrenal glands, and fetal tissues. We demonstrate that the hABC1 expression is induced during differentiation of **human** monocytes into macrophages in vitro. In macrophages, both the hABC1 mRNA and protein expression are upregulated in the presence of acetylated low-density lipoprotein (AcLDL). The AcLDL-induced increase in hABC1 expression is reversed by cholesterol depletion mediated by the addition of high-density lipoprotein (HDL3). Our data, demonstrating sterol-dependent regulation of hABC1 in **human** monocytes/macrophages, suggest a novel role for this transporter molecule in membrane lipid transport.

L5 ANSWER 17 OF 34 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 1998443449 MEDLINE
DOCUMENT NUMBER: 98443449 PubMed ID: 9756759
TITLE: Rapid, transient fluconazole resistance in Candida albicans is associated with increased mRNA levels of CDR.
COMMENT: Erratum in: Antimicrob Agents Chemother 1999 Feb;43(2):438
Erratum in: Rustad T[corrected to Rustad TR]
AUTHOR: Marr K A; Lyons C N; Rustad T R; Bowden R A; White T C; Rustad T
CORPORATE SOURCE: Department of Medicine, University of Washington, Fred Hutchinson Cancer Research Center, Seattle, WA 98109, USA.. kmarr@u.washington.edu
CONTRACT NUMBER: 2T32 AI108044-21 (NIAID)
CA18029 22 (NCI)
R01 DE11367 (NIDCR)
SOURCE: ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, (1998 Oct) 42 (10) 2584-9.
Journal code: 6HK; 0315061. ISSN: 0066-4804.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 20000303
Entered Medline: 19981109
AB Fluconazole-resistant Candida albicans, a cause of recurrent oropharyngeal candidiasis in patients with **human** immunodeficiency virus infection, has recently emerged as a cause of candidiasis in patients receiving cancer chemotherapy and marrow transplantation (MT). In this study, we performed detailed molecular analyses of a series of C. albicans isolates from an MT patient who developed disseminated candidiasis caused by an azole-resistant strain 2 weeks after initiation of fluconazole prophylaxis (K. A. Marr, T. C. White, J. A. H. vanBurik, and R. A. Bowden, Clin. Infect. Dis. 25:908-910, 1997). DNA sequence analysis of the gene (ERG11) for the azole target enzyme, lanosterol demethylase, revealed no difference between sensitive and resistant isolates. A sterol biosynthesis assay revealed no difference in sterol intermediates between the sensitive and resistant isolates. Northern blotting, performed to quantify mRNA levels of genes encoding enzymes in the ergosterol biosynthesis pathway (ERG7, ERG9, and ERG11) and genes encoding efflux pumps (MDR1, **ABC1**, YCF, and CDR), revealed that azole resistance in this series is associated with increased mRNA levels for members of the ATP **binding** cassette (ABC) transporter superfamily, CDR genes. Serial growth of resistant isolates in azole-free media resulted in an increased susceptibility to azole drugs and corresponding decreased mRNA levels for the CDR genes. These results suggest that C. albicans can become transiently resistant to azole drugs rapidly after exposure to fluconazole, in association with increased expression of ABC transporter efflux pumps.

L5 ANSWER 18 OF 34 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 1998196514 MEDLINE
DOCUMENT NUMBER: 98196514 PubMed ID: 9537224
TITLE: Amplification of the ATP-**binding** cassette 2 transporter gene is functionally linked with enhanced efflux of estramustine in ovarian carcinoma cells.
AUTHOR: Laing N M; Belinsky M G; Kruh G D; Bell D W; Boyd J T;

Barone L; Testa J R; Tew K D
CORPORATE SOURCE: Department of Pharmacology, Fox Chase Cancer Center, Philadelphia, Pennsylvania 19111, USA.
CONTRACT NUMBER: CA06927 (NCI)
CA53893 (NCI)
RR05539 (NCRR)
SOURCE: CANCER RESEARCH, (1998 Apr 1) 58 (7) 1332-7.
Journal code: CNF; 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 19980422
Last Updated on STN: 19980422
Entered Medline: 19980416
AB An estramustine-resistant **human** ovarian carcinoma cell line, SKEM, was generated to explore resistance mechanisms associated with this agent. Cytogenetic analysis revealed that SKEM cells have a homogeneously staining region (hsr) at chromosome 9q34. Microdissection of the hsr, followed by fluorescence in situ hybridization to SKEM and normal metaphase spreads, confirmed that the amplified region was derived from sequences from 9q34. In situ hybridization with a probe specific for ABC2, a gene located at 9q34 that encodes an ATP-**binding** cassette 2 (ABC2) transporter, indicated that this gene is amplified approximately 6-fold in the estramustine-resistant cells. Southern analysis confirmed that ABC2 was amplified in SKEM, and Northern analysis indicated that the ABC2 transcript was overexpressed approximately 5-fold. The **ABC1** gene located at 9q22-31 was not amplified in the resistant cells, and mRNA levels of several other ABC transporter genes were unaltered. Consistent with the concept that increased ABC2 expression contributes to the resistant phenotype, we observed that the rate of efflux of dansylated estramustine was increased in SKEM compared with control cells. In addition, antisense treatment directed toward ABC2 mRNA sensitized the resistant cells to estramustine. Together, these results suggest that amplification and overexpression of ABC2 contributes to estramustine resistance and provides the first indication of a potential cellular function for this product.

L5 ANSWER 19 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:318664 BIOSIS
DOCUMENT NUMBER: PREV199800318664
TITLE: The C. elegans cell corpse engulfment gene ced-7 encodes a protein similar to ABC transporters.
AUTHOR(S): Wu, Yi-Chun; Horvitz, H. Robert (1)
CORPORATE SOURCE: (1) Howard Hughes Med. Inst., Dep. Biol., Mass. Inst. Technol., Cambridge, MA 02139 USA
SOURCE: Cell, (June 12, 1998) Vol. 93, No. 6, pp. 951-960.
ISSN: 0092-8674.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The C. elegans gene ced-7 functions in the engulfment of cell corpses during programmed cell death. We report that the CED-7 protein has sequence similarity to ABC transporters, is broadly expressed during embryogenesis, and is localized to the plasma membrane. Mosaic analysis revealed that ced-7 functions in both dying cells and engulfing cells during the engulfment process. We propose that CED-7 functions to translocate molecules that mediate homotypic adhesion between the cell surfaces of the dying and engulfing cells. Like CED-7, the **mammalian** ABC transporter **ABC1** has been implicated in the engulfment of cell corpses, suggesting that CED-7 and **ABC1** may be functionally similar and that the molecular mechanism underlying cell corpse engulfment during programmed cell death may be conserved from nematodes to mammals.

L5 ANSWER 20 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:98018 BIOSIS
DOCUMENT NUMBER: PREV199900098018
TITLE: Cyclosporines (CS) **inhibit** interleukin-1beta (L-1beta) secretion by the **ABC1** transporter, impair leukemia self-renewal and sensitize AML progenitors to antineoplastics.
AUTHOR(S): List, A. F.; Blinsmann-Gibson, B.; Heaton, R.; Schlegel, S.; Guzman, M.; Futscher, B.
CORPORATE SOURCE: Ariz. Cancer Cent., Univ. Ariz., Tucson, AZ USA
SOURCE: Blood, (Nov. 15, 1998) Vol. 92, No. 10 SUPPL. 1 PART 1-2, pp. 675A.
Meeting Info.: 40th Annual Meeting of the American Society of Hematology Miami Beach, Florida, USA December 4-8, 1998 The American Society of Heamatology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English

L5 ANSWER 21 OF 34 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:35568 CAPLUS
DOCUMENT NUMBER: 130:208700
TITLE: **ABC1**, the **mammalian** homolog of the engulfment gene ced-7, is required during phagocytosis of both necrotic and apoptotic cells
AUTHOR(S): Moynault, A.; Luciani, M. F.; Chimini, G.
CORPORATE SOURCE: Centre d'Immunologie, INSERM-CNRS, Marseille, 13288, Fr.
SOURCE: Biochemical Society Transactions (1998), 26(4), 629-635
CODEN: BCSTB5; ISSN: 0300-5127
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Here, the authors provide evidence that the engulfment of necrotic cells is **ABC1** (ATP **binding** cassette transporter)-dependent, because the antibody-mediated steric blockade and the pharmacol. **inhibition** of its function led to an impairment of phagocytosis of both apoptotic and necrotic cells. This, together with the fact that

phagocytosis of both particles is **inhibited** by interference with phosphatidylserine or CD36 recognition, suggests that a similar recognition app. is recruited for the clearance of corpses resulting from degenerative and apoptotic cell death.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 22 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:480896 BIOSIS
DOCUMENT NUMBER: PREV199800480896
TITLE: Effect of CRF and related peptides on calcium signaling in **human** and rodent melanoma cells.
AUTHOR(S): Fazal, Nadeem; Slominski, Andrzej (1); Choudhry, Mashkoor A.; Wei, Edward T.; Sayeed, Mohammed M.
CORPORATE SOURCE: (1) Dep. Pathology, Med. Cent., Loyola Univ., 2160 First South Avenue, Maywood, IL 60153 USA
SOURCE: FEBS Letters, (Sept. 18, 1998) Vol. 435, No. 2-3, pp. 187-190.
ISSN: 0014-5793.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Corticotropin releasing factor (CRF) induces a rapid, within seconds, and dose-dependent increase in the intracellular Ca2+ in both **human** and hamster melanoma cells. This effect is **inhibited** by depletion of extracellular calcium using 3 mM EGTA and is attenuated by the CRF receptor antagonist, alpha-helical-CRF(9-41). Other peptides of the CRF superfamily, sauvagine and urocortin, also induce increases in cytoplasmic calcium concentration but at higher concentrations than CRF. We conclude that malignant melanocytes express CRF receptors, which are coupled to **activation** of plasma membrane calcium channels.

L5 ANSWER 23 OF 34 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 1998332725 MEDLINE
DOCUMENT NUMBER: 98332725 PubMed ID: 9666097
TITLE: Organization of the ABCR gene: analysis of promoter and splice junction sequences.
AUTHOR: Allikmets R; Wasserman W W; Hutchinson A; Smallwood P; Nathans J; Rogan P K; Schneider T D; Dean M
CORPORATE SOURCE: Intramural Research Support Program, SAIC-Frederick, Frederick, MD 21702, USA.
CONTRACT NUMBER: CA74683-02 (NCI)
SOURCE: GENE, (1998 Jul 17) 215 (1) 111-22.
Journal code: FOP; 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19980917
Last Updated on STN: 19980917
Entered Medline: 19980904
AB Mutations in the **human** ABCR gene have been associated with the autosomal recessive Stargardt disease (STGD), retinitis pigmentosa (RP19), and cone-rod dystrophy (CRD) and have also been found in a fraction of age-related macular degeneration (AMD) patients. The ABCR gene is a member of the ATP-**binding** cassette (ABC) transporter superfamily and encodes a rod photoreceptor-specific membrane protein. The cytogenetic location of the ABCR gene was refined to 1p22.3-1p22.2. The intron/exon structure was determined for the ABCR gene from overlapping genomic clones. ABCR spans over 100kb and comprises 50 exons. Intron/exon splice site sequences are presented for all exons and analyzed for information content (Ri). Nine splice site sequence variants found in STGD and AMD patients are evaluated as potential mutations. The localization of splice sites reveals a high degree of conservation between other members of the **ABC1** subfamily, e.g. the **mouse Abc1** gene.
Analysis of the 870-bp 5' upstream of the transcription start sequence reveals multiple putative photoreceptor-specific regulatory elements including a novel retina-specific transcription factor **binding** site. These results will be useful in further mutational screening of the ABCR gene in various retinopathies and for determining the substrate and/or function of this photoreceptor-specific ABC transporter.

L5 ANSWER 24 OF 34 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 97248596 MEDLINE
DOCUMENT NUMBER: 97248596 PubMed ID: 9092582
TITLE: The 220-kDa rim protein of retinal rod outer segments is a member of the ABC transporter superfamily.
AUTHOR: Illing M; Molday L L; Molday R S
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, University of British Columbia, British Columbia, Vancouver V6T 1Z3, Canada.
CONTRACT NUMBER: EY 02422 (NEI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Apr 11) 272 (15) 10303-10.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U90126
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970523
Last Updated on STN: 19970523
Entered Medline: 19970515
AB Outer segments of **mammalian** rod photoreceptor cells contain an abundantly expressed membrane protein that migrates with an apparent molecular mass of 220 kDa by SDS-gel electrophoresis. We have purified the bovine protein by immunoaffinity chromatography, determined its primary structure by cDNA cloning and direct peptide sequence analysis, and mapped its distribution in photoreceptors by immunocytochemical and biochemical methods. The full-length cDNA encodes a 2280-amino acid protein (calculated molecular mass of 257 kDa) consisting of two structurally related, tandem arranged halves. Each half consists of a hydrophobic domain containing six putative transmembrane segments followed by an ATP-

binding cassette. A data base homology search showed that the rod outer segment 220-kDa protein is 40-50% identical in amino acid sequence to the **ABC1** and ABC2 proteins cloned from a **mouse** macrophage cell line. Photoaffinity labeling with 8-azido-ATP and nucleotide **inhibition** studies confirmed that both ATP and GTP **bind** to this protein with similar affinities. Concanavalin A labeling and endoglycosidase H digestion indicated that the rod outer segment protein contains at least one carbohydrate chain. Immunocytochemical and biochemical studies have revealed that the 220-kDa glycoprotein is distributed along the rim region and incisures of rod outer segment disc membranes. From these studies we conclude that the 220-kDa glycoprotein of bovine rod outer segment disc membranes or Rim ABC protein is a new member of the superfamily of ABC transporters and is the **mammalian** homolog of the frog photoreceptor rim protein.

L5 ANSWER 25 OF 34 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 1998025873 MEDLINE
DOCUMENT NUMBER: 98025873 PubMed ID: 9376570
TITLE: Interleukin-1beta secretion is impaired by **inhibitors** of the Atp **binding** cassette transporter, **ABC1**.
AUTHOR: Hamon Y; Luciani M F; Becq F; Verrier B; Rubartelli A; Chimini G
CORPORATE SOURCE: Centre d'Immunologie INSERM-CNRS de Marseille-Luminy, France.
SOURCE: BLOOD, (1997 Oct 15) 90 (8) 2911-5.
Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 20000303
Entered Medline: 19971112

AB The production of interleukin-1beta (IL-1beta), a powerful mediator of inflammation, is tightly regulated at several levels. However, in some pathologic conditions, a pharmacologic treatment is required to control the toxicity of excessive extracellular IL-1beta. Because of the heavy side effects of most therapies used in IL-1beta-mediated pathologies, a goal of pharmacologic research is the development of selective anti-IL-1beta drugs. We show here that the sulfonylurea glyburide, currently used in the oral therapy of noninsulin dependent diabetes, is an **inhibitor** of IL-1beta secretion from **human** monocytes and **mouse** macrophages. Glyburide reduces dramatically the recovery of extracellular 17-kD IL-1beta in the absence of toxic effects on the cells and without affecting the synthesis or processing of the IL-1beta precursor. IL-1beta belongs to the family of leaderless secretory proteins released from the cell by a nonclassical secretory route. In bacteria and yeast Atp **binding** cassette (ABC) transporters are involved in the secretion of leaderless secretory proteins. Interestingly, glyburide blocks the anion exchanger function of **ABC1**, a **mammalian** member of the family of ABC transporters. We thus investigated the involvement of **ABC1** in IL-1beta secretion, through the analysis of the effects of drugs known to **inhibit** IL-1beta secretion, on the activity of **ABC1** and in turn the ability of known **inhibitors** of **ABC1** of blocking IL-1beta secretion. Our data show that IL-1beta secretion and the function of **ABC1** as an anion exchanger are sensitive to the same drugs, therefore suggesting an involvement of the **ABC1** transporter in the secretion of leaderless proteins in mammals.

L5 ANSWER 26 OF 34 MEDLINE
ACCESSION NUMBER: 97160572 MEDLINE
DOCUMENT NUMBER: 97160572 PubMed ID: 9006906
TITLE: **ABC1**, an ATP **binding** cassette transporter required for phagocytosis of apoptotic cells, generates a regulated anion flux after expression in Xenopus laevis oocytes.
AUTHOR: Becq F; Hamon Y; Bajetto A; Gola M; Verrier B; Chimini G
CORPORATE SOURCE: Laboratoire de Neurobiologie Cellulaire, CNRS, 31 Chemin J. Aiguier, 13402 Marseille Cedex 20, France.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Jan 31) 272 (5) 2695-9.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-X75926
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970321
Last Updated on STN: 19980206
Entered Medline: 19970313

AB The ATP **binding** cassette transporter **ABC1** is a 220-kDa glycoprotein expressed by macrophages and required for engulfment of cells undergoing programmed cell death. Since members of this family of proteins such as P-glycoprotein and cystic fibrosis transmembrane conductance regulator share the ability to transport anions, we have investigated the transport capability of **ABC1** expressed in Xenopus oocytes using iodide efflux and voltage-clamp techniques. We report here that **ABC1** generates an anion flux sensitive to glibenclamide, sulfobromophthalein, and blockers of anion transporters. The anion flux generated by **ABC1** is up-regulated by orthovanadate, cAMP, protein kinase A, and okadaic acid. In other ABC transporters, mutating the conserved lysine in the nucleotide **binding** folds was found to severely reduce or abolish hydrolysis of ATP, which in turn altered the activity of the transporter. In **ABC1**, replacement of the conserved lysine 1892 in the Walker A motif of the second nucleotide **binding** fold increased the basal ionic flux, did not alter the pharmacological **inhibitory** profile, but abolished the response to orthovanadate and cAMP agonists. Therefore, we conclude that **ABC1** is a cAMP-dependent and sulfonylurea-sensitive anion transporter.

L5 ANSWER 27 OF 34 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 97179225 MEDLINE
DOCUMENT NUMBER: 97179225 PubMed ID: 9027511
TITLE: The cloning of a **human** ABC gene (ABC3) mapping to chromosome 16p13.3.
AUTHOR: Connors T D; Van Raay T J; Petry L R; Klinger K W; Landes G M; Burn T C
CORPORATE SOURCE: Department of Human Genetics, Genzyme Genetics, Framingham, Massachusetts 01701, USA.
CONTRACT NUMBER: DK44853 (NIDDK)
SOURCE: GENOMICS, (1997 Jan 15) 39 (2) 231-4.
Journal code: GEN; 8800135. ISSN: 0888-7543.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U78735
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970414
Last Updated on STN: 19970414
Entered Medline: 19970331
AB The ATP **binding** cassette (ABC) transporters, or traffic ATPases, constitute a large family of proteins responsible for the transport of a wide variety of substrates across cell membranes in both prokaryotic and eukaryotic cells. We describe a **human** ABC protein with regions of strong homology to the recently described **murine ABC1** and ABC2 transporters. The gene for this novel protein, **human** ABC3, maps near the polycystic kidney disease type 1 (PKD1) gene on chromosome 16p13.3. The ABC3 gene is expressed at highest levels in lung compared to other tissues.

L5 ANSWER 28 OF 34 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:733659 CAPLUS
DOCUMENT NUMBER: 128:20886
TITLE: **Mammalian** ABC transporters and leaderless secretion: facts and speculations
AUTHOR(S): Hamon, Yannick; Luciani, Marie Francoise; Chimini, Giovanna
CORPORATE SOURCE: Centre d'Immunologie, INSERM-CNRS, de Marseille Luminy, Fr.
SOURCE: Unusual Secretory Pathways (1997), 137-159.
Editor(s): Kuchler, Karl; Rubartelli, Anna; Holland, Barry. Landes: Austin, Tex.
CODEN: 65GXA6
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 102 refs., summarizing the general features of **mammalian** ABC transporters, and focusing on a novel ABC transporter, cloned and characterized in the authors' lab, and its involvement in leaderless secretion.

L5 ANSWER 29 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:137072 BIOSIS
DOCUMENT NUMBER: PREV199799436275
TITLE: The engulfment of apoptotic corpses by macrophages require the function of the ATP **binding** cassette transporter **ABC1**.
AUTHOR(S): Luciani, M. F.; Broccardo, C.; Hamon, Y.; Becq, F.; Chimini, G.
CORPORATE SOURCE: Centre d'Immunologie Marseille-Luminy, Case 906, 13288 Marseille, Cedex 9 France
SOURCE: Biochemical Society Transactions, (1996) Vol. 24, No. 4, pp. 565S.
Meeting Info.: 4th International Union of Biochemistry and Molecular Biology Conference Edinburgh, Scotland, UK July 14-17, 1996
ISSN: 0300-5127.
DOCUMENT TYPE: Conference; Abstract; Conference
LANGUAGE: English

L5 ANSWER 30 OF 34 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 96178218 MEDLINE
DOCUMENT NUMBER: 96178218 PubMed ID: 8617198
TITLE: The ATP **binding** cassette transporter **ABC1**, is required for the engulfment of corpses generated by apoptotic cell death.
AUTHOR: Luciani M F; Chimini G
CORPORATE SOURCE: Centre d'Immunologie INSERM CNRS de Marseille-Luminy, 13288 Marseille Cedex 9, France.
SOURCE: EMBO JOURNAL, (1996 Jan 15) 15 (2) 226-35.
Journal code: EMB; 8208664. ISSN: 0261-4189.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960620
Last Updated on STN: 19980206
Entered Medline: 19960613
AB ATP **binding** cassette (ABC) transporters define a family of proteins with strong structural similarities conserved across evolution and devoted to the translocation of a variety of substrates across cell membranes. A few members of the family are known in mammals, but although all of them are medically relevant proteins, knowledge of their molecular function remains scanty. We report here a morphological and functional study of the recently identified **mammalian** ABC transporter, **ABC1**. Its expression during embryonic development correlates spatially and temporally with the areas of programmed cell death. More specifically, **ABC1** is expressed in macrophages engaged in the engulfment and clearance of dead cells. Moreover, **ABC1** transporter is required for engulfment since the ability of macrophages to ingest apoptotic bodies is severely impaired after antibody-mediated steric blockade of **ABC1**. A structural homologue of **ABC1**

has been identified in the Caenorhabditis elegans genome and maps close to the ced-7 locus. Since ced-7 phenotype is precisely defined by an imparied engulfment of cell corpses, it is tempting to surmise that **ABC1** might be a **mammalian** homologue of ced-7.

L5 ANSWER 31 OF 34 MEDLINE DUPLICATE 16
ACCESSION NUMBER: 96242153 MEDLINE
DOCUMENT NUMBER: 96242153 PubMed ID: 8668131
TITLE: Cloning by functional complementation, and inactivation, of the Schizosaccharomyces pombe homologue of the Saccharomyces cerevisiae gene **ABC1**.
AUTHOR: Bonnefoy N; Kermorgant M; Brivet-Chevillotte P; Dujardin G
CORPORATE SOURCE: Centre de Genetique Moleculaire, Laboratoire propre du C.N.R.S. associe a l'universite Pierre et Marie Curie, Gif-sur-Yvette, France.
SOURCE: MOLECULAR AND GENERAL GENETICS, (1996 May 23) 251 (2) 204-10.
Journal code: NGP; 0125036. ISSN: 0026-8925.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-X91616
ENTRY MONTH: 199608
ENTRY DATE: Entered STN: 19960819
Last Updated on STN: 19980206
Entered Medline: 19960805
AB The Saccharomyces cerevisiae gene **ABC1** is required for the correct functioning of the bc1 complex of the mitochondrial respiratory chain. By functional complementation of a S. cerevisiae **abc1**(-) mutant, we have cloned a Schizosaccharomyces pombe cDNA, whose predicted product is 50% identical to the **Abc1** protein. Significant homology is also observed with bacterial, nematode, and even **human** amino acid sequences of unknown function, suggesting that the **Abc1** protein is conserved through evolution. The cloned cDNA corresponds to a single S. pombe gene abc1Sp, located on chromosome II, expression of which is not regulated by the carbon source. Inactivation of the abc1Sp gene by homologous gene replacement causes a respiratory deficiency which is efficiently rescued by the expression of the S. cerevisiae **ABC1** gene. The inactivated strain shows a drastic decrease in the bc1 complex activity. a decrease in cytochrome aa3 and a slow growth phenotype. To our knowledge, this is the first example of the inactivation of a respiratory gene in S. pombe. Our results highlight the fact that S. pombe growth is highly dependent upon respiration, and that S. pombe could represent a valuable model for studying nucleo-mitochondrial **interactions** in higher eukaryotes.

L5 ANSWER 32 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:49766 BIOSIS
DOCUMENT NUMBER: PREV199799348969
TITLE: The engulfment of apoptotic corpses by macrophages requires the function of the ATP **binding** cassette transporter **ABC1**.
AUTHOR(S): Luciani, M. F.; Broccardo, C.; Hamon, Y.; Becq, F.; Chimini, G.
CORPORATE SOURCE: Cantre Immunol. de Marseille-Luminy, Case 906, 13288 Marseille, Cedex 9 France
SOURCE: European Journal of Haematology, (1996) Vol. 57, No. 59 SUPPL., pp. 26.
Meeting Info.: 2nd International Congress of Phagocytes, Biological and Clinical Aspects Pavia, Italy September 4-7, 1996
ISSN: 0902-4441.
DOCUMENT TYPE: Conference; Abstract
LANGUAGE: English

L5 ANSWER 33 OF 34 MEDLINE DUPLICATE 17
ACCESSION NUMBER: 94375008 MEDLINE
DOCUMENT NUMBER: 94375008 PubMed ID: 8088782
TITLE: Cloning of two novel ABC transporters mapping on **human** chromosome 9.
AUTHOR: Luciani M F; Denizot F; Savary S; Mattei M G; Chimini G
CORPORATE SOURCE: Centre d'Immunologie, INSERM-CNRS de Marseille-Luminy, France.
SOURCE: GENOMICS, (1994 May 1) 21 (1) 150-9.
Journal code: GEN; 8800135. ISSN: 0888-7543.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-X75926; GENBANK-X75927; SWISSPROT-P06795; SWISSPROT-P08716; SWISSPROT-P21440; SWISSPROT-P21958; SWISSPROT-P23361; SWISSPROT-P23703
ENTRY MONTH: 199410
ENTRY DATE: Entered STN: 19941031
Last Updated on STN: 19980206
Entered Medline: 19941019
AB The family of ATP **binding** cassette (ABC) transporters or traffic ATPases is composed of several membrane-associated proteins that transport a great variety of solutes across cellular membranes. Two novel **mammalian** members of the family, **ABC1** and ABC2, have been identified by a PCR-based approach. They belong to a group of traffic ATPases encoded as a single multifunctional protein, such as CFTR, STE 6, and P-glycoproteins. Their peculiar structural features and close relationship to ABC transporters involved in nodulation suggest that **ABC1** and ABC2 define a novel subgroup of **mammalian** traffic ATPases.

L5 ANSWER 34 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1993:318599 BIOSIS
DOCUMENT NUMBER: PREV199396026949
TITLE: Differential expression of the common beta and specific alpha chains of the receptors for GM-CSF, IL-3, and IL-5 in endothelial cells.

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AB The present study was designed to reexamine the **interaction** of granulocyte-macrophage colony-stimulating factor (GM-CSF) with endothelial cells (EC) and to investigate the expression of CSF receptor chains in these cells. In agreement with previous data, GM-CSF induced directional migration and, to a lesser degree, proliferation of **human** umbilical vein EC. When compared to basic fibroblast growth factor, GM-CSF was comparable in terms of chemotactic activity and was substantially less active in terms of proliferation. **Binding** studies confirmed the presence of receptors for GM-CSF (GM-CSFR) on EC. The expression of the beta chain common to the GM-CSFR, IL-3 receptor, and IL-5 receptor, as well as of the individual alpha chains, was studied by Northern analysis and/or reverse transcription and polymerase chain reaction. EC expressed high levels of the common beta chain transcripts. Expression of the alpha(GM) and alpha(IL-5) chain mRNA was minimal or absent in normal EC, though the transformed ECV304 endothelial cell line had substantial amounts of alpha(GM) chain mRNA. Unexpectedly, EC expressed alpha(IL-3) chain transcripts. IL-3 induced migration of EC across polycarbonate filters, whereas IL-5 was inactive.